Session IX

Apoptosis and Neurodegenerative Disorders

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Apoptotic components appear following transient cerebral ischemia in rats

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Transient forebrain ischemic studies have been undertaken to examine a time course of appearance of DNA damage following 12 min of 2 vessel occlusion. The breaks in DNA appeared selectively by day 1 in the striatum and by day 2 in the CA1 region of the hippocampus. Double labelling for both DNA breaks and GFAP showed that hippocampal DNA damage was confined to CA1 neurons. The DNA damage consisted of laddered fragments indicative of an ordered apoptotic type of cleavage which persisted without smearing for a week. Decapitation ischemia, a model of pan-necrosis, which also showed DNA breaks by *in situ* end-labelling, in contrast showed smeared random DNA fragments after gel electrophoresis. Despite the random nature of the necrotic DNA fragmentation, the breaks were similar to those of transient ischemia with the predomination of 3′–OH ends with little or no 5′–OH ends being detectable. The large DNA fragments produced in the early stages of chromatin breakdown were studied by pulse field gel electrophoresis. A large DNA fragment of 50 kb was detected by 6 h of reperfusion after 2VO and predominated by 20 h. It was concluded that, despite the lack of apoptotic morphology in the ischemic neurons, the endonucleolytic cleavage of DNA present in the 2VO ischemic model exhibited the hallmarks of an apoptotic mechanism with no evidence of involvement of random necrosis even at later times.

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